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Space representation in the prefrontal cortex

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ABSTRACT

The representation of space and its function in the prefrontal cortex have been examined using a variety of behavioral tasks. Among them, since the delayed-response task requires the temporary maintenance of spatial information, this task has been used to examine the mechanisms of spatial representation. In addition, the concept of working memory to explain prefrontal functions has helped us to understand the nature and functions of space representation in the prefrontal cortex. The detailed analysis of delay-period activity observed in spatial working memory tasks has provided important information for understanding space representation in the prefrontal cortex. Directional delay-period activity has been shown to be a neural correlate of the mechanism for temporarily maintaining information and represent spatial information for the visual cue and the saccade. In addition, many task-related prefrontal neurons exhibit spatially selective activities. These neurons are also important components of spatial information processing. In fact, information flow from sensory-related neurons to motor-related neurons has been demonstrated, along with a change in spatial representation as the trial progresses. The dynamic functional interactions among neurons exhibiting different task-related activities and representing different aspects of information could play an essential role in information processing. In addition, information provided from other cortical or subcortical areas might also be necessary for the representation of space in the prefrontal cortex. To better understand the representation of space and its function in the prefrontal cortex, we need to understand the nature of functional interactions between the prefrontal cortex and other cortical and subcortical areas.

Contents

Abbreviations: ODR, oculomotor delayed-response task; R-ODR, rotatory oculomotor delayed-response task; FT, fixation target; MD, the mediodorsal nucleus of the thalamus.

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1. Introduction

The prefrontal cortex, and especially the dorsolateral prefrontal cortex, has been shown to participate in spatial information processing. This has been demonstrated by lesion studies in which monkeys with bilateral lesions in the dorsolateral prefrontal cortex exhibited severe impairments in the performance of the delayed-response task and the spatial delayed alternation task, but not in the visual discrimination task, the delayed matching-to-sample task, or the delayed object alternation task (e.g., Fuster, 2008; Goldman-Rakic, 1987; Rosenkilde, 1979). In the former tasks, subjects are required to maintain spatial information regarding the visual cue to make a correct behavioral response, while in the latter tasks, subjects are required to maintain non-spatial information regarding the visual cue (e.g., the object itself or the color or shape of the object). Therefore, the dorsolateral prefrontal cortex has been thought to play an important role in maintaining spatial information and using this information to guide a correct response. This prefrontal function has been referred to as spatial working memory by Goldman-Rakic (1987, 1996a).

Prefrontal participation in spatial working memory processes has been examined extensively. In addition to lesions, temporary dysfunction caused by a local injection of chemical (e.g., muscimol) into the prefrontal cortex has also been shown to impair visuospatial working memory in monkeys (Sawaguchi and Iba, 2001). Further, functional brain imaging studies using human subjects have shown activation of the lateral prefrontal cortex while subjects performed spatial working memory tasks (D'Esposito et al., 1998, 2000; Jonides et al., 1993; McCarthy et al., 1994). Evidence that the prefrontal cortex participates in the spatial working memory process has been obtained not only in monkey experiments, but also in rat experiments (Horst and Laubach, 2009).

Neurophysiological studies using monkeys have shown that many prefrontal neurons exhibit tonic sustained excitatory activity during the delay period of spatial working memory tasks, and this activity has been called delay-period activity (e.g., Funahashi et al., 1989). Based on the characteristics of delay-period activity, this activity has been considered to be a neural correlate of a mechanism for temporarily maintaining information (Funahashi, 2001; Funahashi and Kubota, 1994; Fuster, 2008; Goldman-Rakic, 1987; Miller, 2000; Miller and Cohen, 2001; Petrides, 1994). Persistent activity during the delay period has also been observed during spatial working memory performance in human functional brain imaging studies (Curtis and D'Esposito, 2003). Thus, the prefrontal cortex, especially the dorsolateral prefrontal cortex, plays an important role in spatial working memory processes. Persistent delay-period activity is an important neural component for understanding spatial representation by prefrontal neurons. Therefore, a detailed examination of the characteristics of delay-period activity should provide important information regarding how prefrontal neurons represent and process spatial information.

However, delay-period activity can be observed not only during spatial working memory tasks, but also during non-spatial working memory tasks. In addition, delay-period activity participates not only in working memory processes, but also in the processing of information for other cognitive functions. These include the prospective use of information for behavior (Passingham and Sakai, 2004), establishing response selection (Rowe et al., 2000) or a cognitive set (Rowe et al., 2007), spatial attention (Buschman and Miller, 2007; Ikkai and Curtis, 2011; Messinger et al., 2009), and behavioral rules (Wallis et al., 2001; White and Wise, 1999). Spatial information processes are part of most of these cognitive functions and these cognitive functions cannot be separated from spatial information processes. Therefore, a detailed examination of the characteristics of prefrontal neural activity should provide important information regarding how spatial information is represented and how spatial information interacts with non-spatial information and participates in a variety of cognitive functions including working memory.

2. Behavioral paradigms that examine the representation of space in the prefrontal cortex

Since Jacobsen (1936) first reported that monkeys with bilateral lesions of the prefrontal cortex exhibited impairment in delayed-response performance, the delayed-response task had been widely used to examine spatial representations in the prefrontal cortex. This is because the construction and maintenance of the internal representation of spatial information (e.g., memory of the baiting position) are crucial for the correct performance of the delayed-response task and because the impairment of delayed-response performance by bilateral lesions of the lateral prefrontal cortex has been repeatedly confirmed by many lesion studies using monkeys (see Fuster, 2008). Originally, hand-reaching behavior toward a baiting position or a response panel was used as the response behavior. However, saccadic eye movements are now often used as the response behavior. In addition to the delayed-response task, space representation and its function in the prefrontal cortex have been examined using a variety of behavioral tasks including delayed matching-to-position tasks, spatial attention tasks, sequential response tasks, spatial maze tasks, and delayed conditional response tasks.

2.1. Delayed-response tasks

The delayed-response task has been widely used to examine visuospatial representation in the prefrontal cortex. Originally, the delayed-response task was performed using the Wisconsin general test apparatus (WGTA) (Fig. 1). Hand-reaching behavior toward the baiting position was used as the response behavior. In the WGTA, the monkey is kept in a small cage in the laboratory. The cage is placed at one side of the experimental table. The experimenter sits at the other side of the table and presents cue